A31386-A

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Coller et al.		
Serial No.	:	continuation of U.S.S.N. 09/090,757	Examiner:	T.B.D. (Examiner in parent was L.Helms)
Filed	:	HEREWITH	Group Art Unit:	1642
For	:	METHOD OF INHIBITING ANGIOGENESIS AND TUMOR GROWTH AND PREVENTING TUMOR GROWTH AND METASTASIS		

EXPRESS MAIL NO.: EF321688787US

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Official Action dated February 15, 2001, Applicants submit herewith for filing a Continuation Application of the above-identified patent application. Prior to the examination of this application, please take into consider the following amendments and remarks.

AMENDMENTS

IN THE SPECIFICATION:

Please replace the specification with the enclosed substitute specification.

IN THE CLAIMS:

Please cancel original claims 12-14.

Please amend the claims as follows:

1. (amended) A method for inhibiting angiogenesis in a mammal in need thereof comprising administering to the mammal a monoclonal antibody or antigen-binding fragment thereof which acts as an antagonist of the integrins GPIIb/IIIa($\alpha_{IIb}\beta_3$) and $\alpha_v\beta_3$ in an amount effective to inhibit angiogenesis in said mammal.

2. (amended) The method according to claim 1, in which the antigen-binding fragment is an Fab, Fab', or F(ab')2 fragment or derivative thereof.

3. (amended) The method according to claim 1, in which the monoclonal antibody is selected from the group consisting of monoclonal antibody 7E3, produced by the ATCC 8832 hybridoma cell line and a murine/human chimeric monoclonal antibody or antigen-binding fragment thereof comprising the Fab region of monoclonal antibody 7E3.

4. (amended) The method according to claim 1, in which the monoclonal antibody or antigen-binding fragment thereof (a) reacts with normal human blood platelets and with dog blood platelets; (b) fails to react with thrombasthenia platelets or human platelets whose GPIIb/IIIa complex was dissociated with EDTA; (c) reacts slowly with unactivated human platelets and more rapidly with ADP activated human platelets; (d) blocks the interaction of fibrinogen with platelets induced by ADP; and (e) acts as an antagonist to the integrin $\alpha_v\beta_3$ by inhibiting the binding of extracellular matrix ligands to integrin $\alpha_v\beta_3$ and preventing the $\alpha_v\beta_3$ dependent attachment of cells to extracellular matrix protein ligands.

5. (amended) The method according to claim 1, in which the monoclonal antibody or antigen-binding fragment thereof is administered intravenously.

6. (amended) The method according to claim 1, in which the monoclonal antibody or antigen-binding fragment thereof is administered in the amount of about 0.25 mg/kg body weight.

7. (amended) The method according to claim 1, in which the monoclonal antibody or antigen-binding fragment thereof is administered in the amount of about 0.25 mg/kg body weight followed by an infusion of 0.125 mg/kg/min of said antibody.

10. (amended) The method according to claim 1, in which said monoclonal antibody or antigen-binding fragment thereof treats an inflammatory disease.

11. (amended) The method according to claim 1, in which said monoclonal antibody or antigen-binding fragment thereof treats an inflammatory disease selected from the group consisting of rheumatoid arthritis, macular degeneration, psoriasis, diabetic retinopathy.

IN THE DRAWINGS:

Please replace the original informal drawings with with the formal drawings submitted herewith.

REMARKS

Claims 1-11 are pending. Original claims 12-14 are cancelled as having been subject to a restriction requirement in the parent application and to expedite the prosecution of the claims pending in the parent application. Claims 12-14 are cancelled without prejudice to the prosecution of their subject matter in other patent applications.

The originally filed specification is replaced by the substitute specification enclosed herewith. The substitute specification contains amendments to provide paragraph numbering, to revise reference to the Figures, to include sequence listing identifiers and to append a Sequence Listing, to include reference to a grant application and governement rights, and to refer to the parent priority document to establish priority benefits. According to 37 C.F.R. §1.121(b)(3), Applicants enclose herewith, in addition to the substitute specification, a separate specification marked to show changes. Applicants also enclose a computer diskette containing an electronic copy of the Sequence Listing. The contents of the paper and computer readable versions of the Sequence Listing are the same and contain no new matter.

The claims are amended to more particularly state and definitely claim the subject matter which Applicants regard as their invention. Pursuant to 37 C.F.R. §1.121(c)(1), Applicants enclose herewith, on separate sheets, a version of the claims marked to show amendments.

Formal drawings are submitted herewith to replace the originally filed informal drawings. The formal drawings do not contain new matter.

None of the amendments to either the claims or to the specification consitute new matter. An early allowance is earnestly requested.

Respectfully submitted,

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CLAIMS AMENDED TO SHOW CHANGES

1. (amended) A method for inhibiting angiogenesis in a mammal in need thereof comprising administering to the mammal a monoclonal antibody or antigen-binding fragment thereof which acts as an antagonist of the integrins GPIIb/IIIa($\alpha_{IIb}\beta_3$) and $\alpha_v\beta_3$ in an amount effective to inhibit angiogenesis in said mammal.

2. (amended) The method according to claim 1, in which the [antibody] antigen-binding fragment is an Fab, Fab', or F(ab')2 fragment or derivative thereof.

3. (amended) The method according to claim 1, in which the monoclonal antibody is selected from the group consisting of [has the identifying characteristics of] monoclonal antibody 7E3, produced by the ATCC 8832 hybridoma cell line and a murine/human chimeric monoclonal antibody or antigen-binding fragment thereof comprising the Fab region of monoclonal antibody 7E3.

4. (amended) The method according to claim 1, in which the monoclonal antibody [has the identifying characteristics of monoclonal antibody c7E3] or antigen-binding fragment thereof (a) reacts with normal human blood platelets and with dog blood platelets; (b) fails to react with thrombasthenia platelets or human platelets whose GPIIb/IIIa complex was dissociated with EDTA; (c) reacts slowly with unactivated human platelets and more rapidly with ADP activated human platelets; (d) blocks the interaction of fibrinogen with platelets induced by ADP; and (e) acts as an antagonist to the integrin $\alpha_v\beta_3$ by inhibiting the binding of extracellular matrix ligands to integrin $\alpha_v\beta_3$

and preventing the $\alpha_v\beta_3$ dependent attachment of cells to extracellular matrix protein ligands.

5. (amended) The method according to claim 1, in which the monoclonal antibody or antigen-binding fragment thereof is administered intravenously.

6. (amended) The method according to claim 1, in which the monoclonal antibody or antigen-binding fragment thereof is administered in the amount of about 0.25 mg/kg body weight.

7. (amended) The method according to claim 1, in which the monoclonal antibody or antigen-binding fragment thereof is administered in the amount of about 0.25 mg/kg body weight followed by an infusion of 0.125 mg/kg/min of said antibody.

10. (amended) The method according to claim 1, in which said monoclonal antibody or antigen-binding fragment thereof treats an inflammatory disease.

11. (amended) The method according to claim 1, in which said monoclonal antibody or antigen-binding fragment thereof treats an inflammatory disease selected from the group consisting of rheumatoid arthritis, macular degeneration, psoriasis, diabetic retinopathy.

PENDING CLAIMS

1. (amended) A method for inhibiting angiogenesis in a mammal in need thereof comprising administering to the mammal a monoclonal antibody or antigen-binding fragment thereof which acts as an antagonist of the integrins GPIIb/IIIa($\alpha_{IIb}\beta_3$) and $\alpha_v\beta_3$ in an amount effective to inhibit angiogenesis in said mammal.

2. (amended) The method according to claim 1, in which the antigen-binding fragment is an Fab, Fab', or F(ab')2 fragment or derivative thereof.

3. (amended) The method according to claim 1, in which the monoclonal antibody is selected from the group consisting of monoclonal antibody 7E3, produced by the ATCC 8832 hybridoma cell line and a murine/human chimeric monoclonal antibody or antigen-binding fragment thereof comprising the Fab region of monoclonal antibody 7E3.

4. (amended) The method according to claim 1, in which the monoclonal antibody or antigen-binding fragment thereof (a) reacts with normal human blood platelets and with dog blood platelets; (b) fails to react with thrombasthenia platelets or human platelets whose GPIIb/IIIa complex was dissociated with EDTA; (c) reacts slowly with unactivated human platelets and more rapidly with ADP activated human platelets; (d) blocks the interaction of fibrinogen with platelets induced by ADP; and (e) acts as an antagonist to the integrin $\alpha_v\beta_3$ by inhibiting the binding of extracellular matrix ligands to integrin $\alpha_v\beta_3$ and preventing the $\alpha_v\beta_3$ dependent attachment of cells to extracellular matrix protein ligands.

5. (amended) The method according to claim 1, in which the monoclonal antibody or antigen-binding fragment thereof is administered intravenously.

6. (amended) The method according to claim 1, in which the monoclonal antibody or antigen-binding fragment thereof is administered in the amount of about 0.25 mg/kg body weight.

7. (amended) The method according to claim 1, in which the monoclonal antibody or antigen-binding fragment thereof is administered in the amount of about 0.25 mg/kg body weight followed by an infusion of 0.125 mg/kg/min of said antibody.

8. The method according to claim 1, in which the mammal is selected from the group consisting of a primate, dog, cat, and human.

9. The method according to claim 1, in which the mammal is a human patient.

10. (amended) The method according to claim 1, in which said monoclonal antibody or antigen-binding fragment thereof treats an inflammatory disease.

11. (amended) The method according to claim 1, in which said monoclonal antibody or antigen-binding fragment thereof treats an inflammatory disease selected from the

group consisting of rheumatoid arthritis, macular degeneration, psoriasis, diabetic retinopathy.